REMARKS

The Office Action

Applicants' specification was objected to under 37 C.F.R. §§ 1.821–1.825. Claims 1-8, 10-12, and 14-23 were rejected under 35 U.S.C. § 112, first paragraph. Claims 1-8, 11-12, and 14-23 were rejected under 35 U.S.C. § 112, second paragraph. Claims 1-4, 6-7, 11, 14, 16, and 20-21 were rejected under 35 U.S.C. § 102(a), and claims 1-8, 10-12, and 14-23 were rejected under 35 U.S.C. § 103(a). Each of these rejections is addressed as follows.

Sequence Listing

Applicants have amended the application to include sequence identifiers for the sequences disclosed in the specification and, in the accompanying Statement under 37 C.F.R. §§ 1.821-1.825, submit a sequence listing in accordance with the requirements set forth in 37 C.F.R. §§ 1.821-1.825. No new matter has been added by these amendments.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-8, 10-12, and 14-23 stand rejected under 35 U.S.C. § 112, first paragraph, on the ground that the recitation of the word "soluble" is considered new matter. To expedite allowance, Applicants have deleted the word "soluble" from the claims, rendering the rejection moot. For the record, Applicants disagree with the basis

for the rejection of these claims, and Applicants reserve the right to pursue all canceled subject matter in this or future continuing applications.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-8, 11-12, and 14-23 were rejected, under 35 U.S.C. § 112, second paragraph on the basis that certain claim terms are indefinite.

In particular, with respect to claims 1, 6, 11, and 12, the Office asserts that the phrase "Sendai virus vector expressing" is unclear and confusing. To address this rejection, Applicants have amended these claims to refer to a "recombinant Sendai virus vector comprising a gene encoding a chemokine, wherein said vector, when transfected to a host, expresses the chemokine in a biologically active form." In addition, claim 6 has been amended to include the step of "introducing said vector into a host cell, allowing the vector to produce the chemokine." This rejection may be withdrawn.

Claims 8, 17, and 18 were rejected on the basis that there is insufficient antecedent basis for the phrase "removing virion." Applicants have amended these claims to correct the antecedent basis for the phrase in question. This basis for the rejection may be withdrawn.

In addition, claims 15, 22, and 23 were deemed vague and unclear in reciting the phrase "inhibiting proliferation of HIV-infected cells." These claims have now been amended to recite "wherein said chemokine inhibits proliferation of HIV-infected cells *in*

vitro," and this ground of rejection may be withdrawn.

Rejection under 35 U.S.C. § 102(a)

Claims 1-4, 6-7, 11, 14, 16, 20-21 were rejected under 35 U.S.C. § 102(a), as being anticipated by Shioda *et al.* (*AIDS Res.* 11:167, 1997). This rejection is respectfully traversed.

The Shioda reference is not prior art to the present invention. Applicants are the joint inventors of the pending claims and are the joint contributors of any relevant information in the Shioda reference, and a Declaration of Yoshiyuki Nagai, a co-inventor of this application, to this effect is attached. Accordingly, the Shioda reference does not constitute prior art in this application (*In re Katz*, 687 F.2d 450 (C.C.P.A. 1982)), and the § 102(a) rejection may be withdrawn.

Rejection Under 35 U.S.C. § 103:

Claims 1-8, 10-12, and 14-23 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Yu *et al.* (*Genes to Cells* 2:457-466, 1997) and Bluel *et al.* (*Nature* 382:829-832, 1996) in view of Hasan *et al.* (*J. Gen. Vir.* 78:2813-2820, 1997) and Czaplewski *et al.* (*J. Biol. Chem.* 274:16077-16084, 1999). This rejection is respectfully traversed.

At the outset, Applicants point out that the claims require that the chemokine produced according to the invention be biologically active.

In maintaining the rejection, the Examiner asserts that

> Yu *et al.* does teach that expression of luciferase resulted in aggregation of the expressed protein, however contrary to the attempt by Yu et al, Hasan *et al.* clearly teach that the Sendai virus is capable expressing an active form of the luciferase protein (see results in Table 2 and Figure 2). It is noted that the present specification provides no specific sequences for the chemokines contemplated or specific vectors, and thus, relies on the art for these teachings. With respect to soluble chemokines, Czaplewski *et al.* teach that chemokines have been generated and that the structure of various chemokines have been characterized in detail indicating that "[N]ot all chemokines self-associate."[citation omitted.]

The Office's understanding of the use of a Sendai virus as an expression system for the production of recombinant proteins is overly simplistic, and assumes that any protein can be easily produced using a Sendai virus-based expression system. In fact this is not the case. As previously noted, Yu had mixed results when expressing recombinant proteins using a Sendai virus-based expression system: Yu produced biologically active gp120, but failed to produce biologically active luciferase. Here the Office fails to explain why expression of biologically active gp120 predicts successful expression of biologically active chemokine using a Sendai virus based expression vector. Moreover, the Yu reference, in view of their failure to produce biologically active luciferase, is further deficient in providing any basis whatsoever for predicting the success of Applicants' claimed methods and compositions. To address Yu's failure to produce

biologically active luciferase, the Examiner turns to Hasan for the proposition that biologically active luciferase was in fact produced. Regarding Hasan, the Office's understanding is incorrect. Hasan does not teach that Sendai viruses are capable of expressing an active form of the luciferase protein.[1] Hasan clearly indicates, for example, at page 2814, right column, that "infected cells were lysed in ... lysis buffer and the enzyme activity ... was measured by a luminometer." In addition, Applicants point out that the Czaplewski *et al.* reference is not available as prior art, since this article, on its face, bears a 1999 publication date, which is after the filing date of the instant application.

The Office also argues that

> chemokines have been successfully produced prior to the filing of the instant application.

The Office fails to cite any references supporting this statement.

The Office further argues that

> the sequences disclosed in the cited references would anticipate the embodiments of the chemokine sequences and vectors required to practice the instantly claimed invention.

Nowhere in the references of record is a Sendai virus vector that includes a gene encoding a chemokine disclosed. Absent such a teaching, the claims cannot be anticipated.

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1 Hasan *et al.* teach the potential utility of Sendai virus vector. In this regard, Hasan discusses some problems of non-segmented negative strand virus including Sendai virus; namely, [t]hat the presence of the additional gene slightly but significantly retarded virus replication and resulted in a several fold decrease in virus yielding during single-cycle growth (page 2819, left column, lines 13-15); the frequency of nucleotide misincorporation in RNA genomes has been estimated to be as high as 10^{-4} to 10^{-5} per site per replication because of the highly error-prone nature of viral RNA-dependent polymerases due to the absence of proofreading and repair mechanisms (page 2819, left column, lines 38-43); and [i]t will be interesting to learn the real limit of inserting into paramyxovirus genomes and how this limit is determined (page 2819, right column, lines 4-6).

Applicants further note that the Office's reliance on Hasan's statement suggesting that the "Sendai virus will be "an excellent tool for foreign gene expression" is taken out of context. The passage of Hasan relied on by the Office refers to influenza A virus, not Sendai virus: "Influenza A virus, a segmented negative-strand RNA virus, is also an excellent tool for foreign gene expression."

Turning to Bluel, Applicants note that Bluel discusses chemokines, but does not discuss using a Sendai virus vector-based expression system. The existence of a reference merely disclosing a chemokine is insufficient, when combined with Yu or Hasan, to support a finding of obviousness. In addition, Bluel adds nothing to the deficiencies of Yu or Hasan, not the motivation to even try synthesizing a chemokine using a Sendai virus based vector. This motivational deficiency is further highlighted by the knowledge understood at the time that production of recombinant proteins using a Sendai virus based expression system was not predictable (compare Yu's production of biologically active gp120 and inactive luciferase). Like Yu and Hasan, Bluel cannot teach what they did not know.

In sum, given the problems associated with expressing proteins using non-segmented negative-strand RNA viruses including Sendai virus and chemokine aggregation, the cited references do not provide "a reasonable expectation of success," which is required to establish a *prima facie* case of obviousness, because nothing in the references taught or suggested that a biologically active chemokine, as is claimed in the

instant application, would result when a Sendai virus-based expression system is employed.

For all of the above reasons, the § 103(a) rejection should be withdrawn.

CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is respectfully requested.

Enclosed is a petition to extend the period for replying for three months, to and including May 20, 2003. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 20 May 2003

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